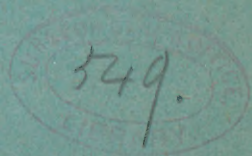




WILLIAMS (F.H.)

*Diphtheria and Other Membranous
Affections of the Throat.*

BY
FRANCIS H. WILLIAMS, M.D.,
OF BOSTON.



FROM
THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES,
NOVEMBER, 1893.

DIPHTHERIA AND OTHER MEMBRANOUS AFFECTIONS OF THE THROAT.¹

BY FRANCIS H. WILLIAMS, M.D.,
OF BOSTON.

IN discussing this subject there are three principal points to which I shall have the pleasure of calling attention. First, the diagnosis of diphtheria by means of the microscope. Second, the coincidence of diphtheria and other diseases. Third, the treatment of diphtheria.

The Report of the State Board of Health for 1891 gives valuable tables prepared with great care by Dr. S. W. Abbott, which show the mortality of various diseases in Massachusetts, from 1871 to 1890 inclusive. From them it may be seen that during these twenty years there were 56,474 deaths from pneumonia; 36,553 deaths from diphtheria and croup; 19,421 deaths from typhoid fever; and 14,639 deaths from scarlet fever. I shall show later, that even this large figure of 36,553 deaths from diphtheria and croup probably does not represent all the fatal cases of membranous throats during the twenty years. Osler states that while other contagious diseases have diminished within the past decade, diphtheria, particularly in cities, has increased. Moreover, the mortality in this disease is very high, from 40 per cent. to 60 per cent. of the patients dying.

Precise discrimination between different kinds of membranous throats was formerly impossible, but within the last ten years, beginning with the careful observations of Klebs and Loeffler, it has been shown that among membranous affections of the throat there is one of supreme importance which is characterized by the presence of an organism known as the Klebs-Loeffler bacillus. There are often other organisms present with this bacillus, but they are not of such serious import. These other organisms, chiefly various forms of cocci, may also be found in the throat without the bacillus, but associated with such appearances that they often cannot be distinguished from those accompanying the bacillus, except by the aid of the microscope. It has been agreed to call the most fatal of these membranous inflammations of the throat, the disease identified by the Klebs-Loeffler bacillus, diphtheria; certain other forms of membranous throats are often designated as pseudo-diphtheria. Let me recall to your minds some of the characteristics of this bacillus disease, diphtheria. In the beginning it is local; the bacilli

¹ Read at the annual meeting of the Massachusetts Medical Society, June 14, 1893.



grow on or in a mucous membrane or wound, at which point a false membrane is formed; they do not as a rule enter the system—although Frosch¹ has found them in various organs of the body in ten out of fifteen autopsies after diphtheria—but their baneful effects are exerted chiefly through a very poisonous substance, diphtherotoxin, which they secrete and which is soluble and readily absorbed. This substance, which is a toxalbumin, has been isolated, and when freed from all bacilli and injected into animals, causes many of the symptoms of diphtheria, such as paralysis, heart failure and local necrosis, but it does not give rise to a false membrane.

The early recognition of a disease so dangerous to the individual and to those near him as diphtheria is of the first importance, and yet by the ordinary methods an early diagnosis is nearly always impossible. It may even in the very early stage be confounded with follicular tonsillitis. Fortunately, we have now in our hands a means of diagnosis which is excellent precisely in the early stage of the disease. It consists in the examination of cultures made from the suspicious throat, and subsequent inoculation of animals; this requires special training and appliances, and it is necessary to wait about twenty hours to learn the result of the cultures, and longer to learn that of the inoculations.

The Boston City Hospital is now erecting much larger buildings for contagious diseases; at present there are two buildings, each containing two wards besides separate rooms devoted to the contagious service, one for diphtheria and the other for scarlet fever. In the diphtheria wards patients when needing tracheotomy or intubation go to the surgical service, the others to the medical service. Beginning with 1891 I have had during medical services in these wards 442 patients; 211 of these had membranous inflammation of the throat; 231 scarlet fever, complicated in 58 cases with severe membranous inflammation of the throat, making in all 269 patients with membranous throats. The diagnosis by cultures, which I initiated at the hospital, was made in 93 of the cases of membranous throats that were under my care during about three months of 1892 and 1893. In 3 of the cases cover-glass preparations only were made. These 96 cases are classed as follows:

TABLE I.

	Cases.	Recovered.	Died.
Diphtheria	40	20	20
Diphtheria and scarlet fever	12	6	6
Diphtheria and measles	1	1	—
Diphtheria and typhoid fever	1	1	—
Pseudo-diphtheria	19	17	2
Pseudo-diphtheria and scarlet fever	23	18	5
	96		

¹ Zeitschrift für Hygiene und Infektionskrankheiten, 1893, Bd. xiii. Heft 1.

These examinations showed that a considerable number of the cases with false membranes that were admitted to the diphtheria ward were not diphtheria, thus demonstrating the necessity for bacteriological examinations. Furthermore, in four of those that were diphtheria there was no membrane in sight. This likewise shows the importance of bacteriological examination where there is the least suspicion of diphtheria.

My plan was to have a sterilized cotton swab rubbed over the throats of all patients coming to the medical side of the diphtheria ward, except those too weak to be disturbed, and over the throats of all those in the scarlet fever ward who might at any time have a deposit in the throat, and cultures were then made, except in a few instances, where cover-glass preparations only were made.

Let me now direct attention to these 96 cases in which the diagnosis was made by means of the microscope, which consist of two series: the first series of 23 cases in 1892, from which the cultures, followed in some cases by inoculation of guinea-pigs, were made for me by Mr. A. P. Mathews, assistant in biology at the Massachusetts Institute of Technology, to whom I am much indebted, and a second series of 73 cases in 1893, for which I enlisted the interest and co-operation of Professor Councilman, under whose direction the cultures were made, and of Dr. E. M. Holden, who gave freely the large amount of time which work of this character requires and on which its success so much depends.

In 49 (Table II.) of the 93 cases I made a preliminary cover-glass examination, when I first saw the patient, from the material adhering to a sterilized cotton swab directly after it had been rubbed over the suspected throat—this examination can be made in a few minutes in the ward or at the patient's house—and on the following day learned the result of the examination made from cultures. If either examination shows the characteristic bacilli every precaution should be taken.

TABLE II.—*Diagnosis of Diphtheria based on Cultures.*

(Both cultures and cover-glass examinations made.)

Diphtheria	20
Diphtheria and scarlet fever	3
Pseudo-diphtheria	8
Pseudo-diphtheria and scarlet fever	10
Tonsillitis	6

47

In 38 of these 47 cases (cases 48 and 49 will be referred to later) the cultures and cover-glass examinations agreed, in 7 disagreed, and in 2 cases the result of the cover-glass examination was doubtful. Two of the 7 cases where the two methods disagreed are classed in the table as pseudo-diphtheria, the bacillus not being found in the cultures, although thought to be present in the cover-glass examinations. These

two patients died. The third case is classed in the table as pseudo-diphtheria and scarlet fever, as the bacilli were not found in the cultures, although thought to be present in the cover-glass examination. The brother of the patient had diphtheria and scarlet fever. In the fourth case, where the two methods disagreed, I probably mistook some other organism for the bacillus on the fourteenth day of the disease. In the three remaining cases I failed to find the bacilli in the cover-glass examination, but they were found in the cultures. In the forty-eighth case, not noted in Table II., the bacilli were found neither in the culture nor in the cover-glass examination, but the patient did not enter the hospital until the thirty-fifth day of the disease; she had post-diphtheritic paralysis on the thirty-third day of the disease.

The preliminary examination is of service when the cover-glass shows abundant and characteristic bacilli; it seems to be more satisfactory in the early than in the later stages of the disease. In the later stages the bacillus is more apt to be obscured by slower-growing organisms; failure to find the bacilli does not establish their absence, and the cover-glass examinations should of course be followed by cultures.

The cultures are not infallible; for some reason, such as the presence of a small quantity of corrosive sublimate, the bacilli may not grow when planted, and therefore may not be found in the cultures. With all the sources of error, however, we now have at our disposal a method of diagnosis far better than anything we have had heretofore, which enables us to recognize early the most dangerous among the acute diseases of the throat which are characterized by a membrane. It is a great relief to the family and friends, as well as to the physician, to have such assurance as this means of diagnosis gives us, that certain apparently most serious cases are not cases of diphtheria. It likewise points out to us mild cases of diphtheria that clinically might be classed as pseudo-diphtheria, but the contagion from which might give rise to a serious illness in another individual. By its aid also we may learn in the future to recognize better the symptoms that distinguish diphtheria from other membranous affections of the throat. Further, it shortens the stay of the patient in the hospital and diminishes the period of convalescence for those who have had only pseudo-diphtheria, as unless we can distinguish between them we are compelled to be over-careful of cases in which the after-effects are not so much to be dreaded. As a rule patients in whose throats the bacillus is not found may get up and go about early, while in the cases of diphtheria one should make haste slowly, as even lifting a child out of its crib to feed it may bring on heart failure some time after the acute symptoms have disappeared. Likewise it may sometimes be of great importance to summon the family or friends from a distance if we are assured early that the disease is a very dangerous one.

Diphtheria usually begins on the tonsils, so far as my experience goes. It is sometimes stated that when the false membrane is limited to the tonsils the disease is not diphtheria, but that if the membrane covers also other parts of the throat the disease probably is diphtheria. Let us consider for a moment what bearing, if any, the distribution of the false membrane has upon the diagnosis. In the 23 cases of scarlet fever complicated with pseudo-diphtheria (Table III.), the membrane was limited to the tonsils in 5 only, and in 3 it had evidently extended to the larynx. In 2 cases of pseudo diphtheria (Table I.) the membrane had also extended to the larynx.¹ These 5 laryngeal cases were children, the eldest of whom was five years old. In 4 of the 40 diphtheria cases (Table I.) there was no membrane in sight; in 5 the membrane when first seen was on the tonsils only, but it spread later to other parts. In one-half of the pseudo-diphtheria cases (Table I.) the membrane was on the tonsils and other parts. These facts show that in making a diagnosis it is not advisable to place reliance upon the distribution of the membrane, although it seems usually to be more widely distributed in diphtheria than in pseudo-diphtheria.

Extreme youth, the presence of membrane in the larynx or even lower, and a weak heart all influence the prognosis most unfavorably.

We now come to the *second* point, the coincidence of diphtheria and other diseases. Let us consider first the coincidence of diphtheria and scarlet fever, the occurrence of which has been questioned and much discussed. In the series of cases of both 1892 and 1893, already alluded to, such association occurred. In 97 of the cases of scarlet fever the diagnosis was made by cultures in all those that had membranous throats. The result was as follows:

TABLE III.

	Cases.	Died.
Scarlet fever	62	8
Scarlet fever and pseudo-diphtheria	23	5
Scarlet fever and diphtheria	12	6
	<hr/> 97	

In one of the 12 cases of diphtheria complicated with scarlet fever diphtheria was followed by scarlet fever, in one preceded by scarlet fever, and in ten cases diphtheria and scarlet fever occurred simultaneously. This class of cases seems to be rapidly increasing in Boston.

A noteworthy point in this table is the fact that there were more deaths among the 35 cases of scarlet fever complicated with membranous throats than in the 62 cases of scarlet fever only: as we should expect, in scarlet fever complicated with diphtheria, it is the Klebs-Loeffler bacillus which is the dangerous factor and which threatens the life of

¹ Intubation or tracheotomy may be required in pseudo-diphtheria.

the patient much more than the scarlet fever. In the light of this experience, a former series of my scarlet-fever cases is interesting. There were 86 in this series, 19 of which were complicated with membranous throats, and 67 were uncomplicated. Of the 67 cases of scarlet fever, 3 died, or 4½ per cent.; of the 19 cases of scarlet fever complicated with membranous throats, 9 died, or 47 per cent., showing in this series also the high mortality of scarlet fever when complicated with membranous throats as compared with scarlet fever only. These cases came under my charge before a diagnosis by cultures was made in this community.

The source of some of the cases noted in Tables I. and III. deserves a word in passing: 35 of them came from two Homes for Children. The first home sent 19 patients to the hospital between February 14th and March 20th, inclusive. The epidemic began with scarlet fever, of which there were 13 cases, and continued with cases of scarlet fever complicated with pseudo-diphtheria, and scarlet fever complicated with diphtheria, and ended with one case of diphtheria alone; this patient was an adult. The second Home for Children sent 16 cases to the hospital, which included the same variety of diseases as the first.

The coincidence of this bacillus with other diseases than scarlet fever is also interesting. In three of the cases diphtheria and measles probably occurred together. Two of these died. The third and only one in which a swab was taken from the throat (Case 49, already alluded to), has a special interest in that the bacilli were detected readily on a cover-glass by both Dr. Councilman and myself, but they failed for some unknown reason to grow in the culture media, although two trials were made. There was abundant opportunity in this case to get some of the membrane, as the child coughed up large pieces of it.

Another case of interest is one in which diphtheria and typhoid fever occurred simultaneously:

L. J., a girl aged seventeen years, well developed and nourished, was ill with cellulitis of the leg, with possible caries of the femur, for some weeks before she came into my service. Five days before entrance she complained of sore-throat, and two days later a membrane was seen in the throat, in which Dr. Councilman found the Klebs-Loeffler bacillus. The membrane was seen for the last time on the eighth day after entrance. On the day of entrance the temperature was 104° to 105°, and the pulse 130 to 140, but on the following day the temperature reached 105° and the pulse 150; one rose spot was found on the abdomen; the number of spots increased daily for seven days, and were unusually numerous and characteristic. The spleen was enlarged, and its lower edge could be felt at the margin of the ribs. Hæmoglobin was 90 per cent., and the number of leucocytes normal, 7500. On the third day the stools were typhoidal and the patient dull. The pulse was 110 to 120, the temperature remained about 104° for a week, and then fell by lysis to normal. Recovery.

These cases suggest a connection between the bacillus of diphtheria and certain of the paralyses which sometimes occur after scarlet fever, measles, and typhoid fever. Furthermore, the mortality from diphtheria in our State should include some of the cases classed under scarlet fever, measles, and typhoid fever, as already suggested.

We now come to the *third* point, namely, the *treatment* of diphtheria, and this subject divides itself naturally into two parts, general and local treatment. The former may be outlined in a few words. The food of the patient deserves special attention. Alcohol is, in some cases, of service. Iron is frequently given for anæmia.

In 19 cases—

Diphtheria	9
Diphtheria and scarlet fever	3
Pseudo-diphtheria	4
Pseudo-diphtheria and scarlet fever	3
	<hr/>
	19

—most of which appeared anæmic, I determined the hæmoglobin by Fleischl's hæmometer, and this instrument did not in the majority of cases confirm the apparent anæmia. Sixteen of these 19 cases, children and adults, had about, and in some cases more than, 100 per cent. of hæmoglobin. The 3 remaining cases were all children. In the first of these, a child five years old, ill with diphtheria, the hæmoglobin was 75 per cent. In the other two, children of a year old, one ill with diphtheria, the other with pseudo-diphtheria, the hæmoglobin was about 50 per cent. Mercury in small doses has been recommended, but it did not seem to me of service in the few cases in which I have used it or seen it used. The cases of Behring treated with the blood-serum of immune animals encourage us to hope that a feasible internal remedy may be found.

At present local remedies are our best means for the treatment of this disease, and obviously they are best adapted to those cases that are seen early, before much of the poison has been absorbed, and further, to cases in which the membrane is accessible.

Given a patient in whose throat is a patch of membrane filled with bacilli that reproduce themselves in a very short period and which generate a soluble and most virulent poison; a membrane that may be thick and tough, and over the surface of which there constantly passes a stream of saliva that will quickly carry away the remedies applied to it; situated in a region to which applications can be made for short intervals only, and even then is not easy of access: what should we do? It is worse than useless to tear off the membrane; this causes bleeding; the membrane rapidly returns, and over a larger area. The bacillus seems, above all things, to delight in the blood-serum, and the

spread of the membrane follows the course of the bleeding as eagerly as a hungry horse will follow oats. Bacteriologists, in searching for a medium in which to tempt the bacillus to grow outside of the body, have found nothing better adapted to the organism than blood-serum.

Chlorate of potash does not seem to me of service and in excessive doses may do serious harm. Nitrate of silver is a caustic that does not penetrate deeply. Chromic acid is one of the most relentless of all caustics. Iodine is irritating when inhaled, as are the vapors from saturated solutions of chlorine. Solutions of carbolic acid are poisonous and inefficient as germicides. I have not succeeded with digestives. *Sesqui-chloride of iron*, often used in the form of a tincture, has been, and with some still is, a favorite application. Knowing that these iron preparations contained free acid, I thought it probable that the acid rather than the iron would prove to be the active agent. To test this, Mr. A. P. Mathews compared for me a solution of chloride of iron with a solution containing no iron, but having the same quantity of acid as in the iron solution. The iron solution was found to be no better as a germicide against the bacillus of diphtheria than the acid water, thus showing the acid to be the essential agent in the iron solution. The *tincture* of the chloride of iron contains 2.5 per cent. to 3.4 per cent. of free hydrochloric acid; the *solution* of chloride of iron contains from 5.4 per cent. to 7.4 per cent. of free hydrochloric acid. These iron solutions are an excessively unpleasant treatment. *Corrosive sublimate* has much reputation as a germicide, but its action seems to be inhibitory rather than germicidal. I insert here three cases of diphtheria, the diagnosis of which was based on cultures, in which corrosive sublimate was used locally, as better treatment was not at the time practicable, and they show how the membrane may persist under its use:

J. B., aged twelve years, entered the hospital on the third day of the disease. Membrane was seen on both tonsils, both sides of pharynx, and a small spot one-eighth of an inch in diameter on posterior pharynx. Klebs-Loeffler bacilli found in culture. The local treatment for thirteen days was corrosive sublimate 1:10,000 in spray every four hours, but in spite of this the membrane continued to cover more area and to become thicker until the eighth day of the disease, when the throat began to clear. Septic odor. On the tenth day, no bacilli were found in culture; their growth was probably inhibited by the presence of corrosive sublimate. On the sixteenth day, the throat was clear. The heart was noticeably weak in its action, and tincture of digitalis was given. After six weeks, the patient left the hospital for the Convalescent Home. There had been nothing seen in the throat for twenty-six days, and she had been about the ward. She passed three weeks in the Convalescent Home, and then on account of hoarseness returned to the hospital. My service was then at an end, but the records, which I have the privilege of inserting here, state that there was "a piece of membrane adherent to one vocal cord. After eleven weeks, the tonsils were large and covered with a whitish film or membrane which could be

wiped off with difficulty; breath foul. Dr. Councilman found Klebs-Loeffler bacilli abundant." The last record of membrane, which was on the tonsils, was almost twelve weeks after the onset of the disease. The patient was discharged on the one hundredth day of the disease.

This case illustrates the futility of the 1 : 10,000 solution of corrosive sublimate in preventing the spread of the membrane, and the persistence of the bacilli in spite of its use. It would be desirable to have bacteriological examinations made of every throat before the patient is allowed to leave the contagious ward, care being taken not to have corrosive sublimate used at the time the swab is rubbed over the throat, as a very small amount of it will inhibit the growth of the bacilli in the culture tubes.¹

In the two following cases the attempt was made to get a cleansing action from a weak (7.5-volume²) solution of hydrogen peroxide to assist the action of the 1 : 10,000 corrosive sublimate.

In the first of these the patient, a woman aged twenty-two years, had paralysis on the fifteenth day of the disease, and the throat was not clear until the seventeenth day of the disease. In the second case, M. McP., a woman aged twenty-eight years, entered the hospital on the third day of the disease. Thick membrane on both sides of the uvula and on the left tonsil. Klebs-Loeffler bacilli found in culture. The local treatment was a spray of 7.5-volume solution of hydrogen peroxide every two hours, followed by a spray of corrosive sublimate 1 : 10,000. On the seventh day of the disease the patient was hoarse and evidently the membrane had spread to the larynx. Prostration. Reduplication of heart sounds. After ten days a spray of corrosive sublimate 1 : 20,000 was used every four hours. Three days later this was omitted, as the patient was salivated. Seventeenth day, paralysis. Thirty-fourth day the throat was clear. The patient was discharged on the forty-first day of the disease.

These cases show that the membrane may not be removed, but may continue to spread under a local treatment of corrosive sublimate 1 : 10,000, as illustrated in J. B., and also when this is used in connec-

¹ Since this paper was read a man has come to the hospital with naso-pharyngeal paralysis. No membrane was seen in the throat by the physicians who examined him, but Klebs-Loeffler bacilli were found in the cultures. The history of the case showed that the attack of diphtheria had begun about eight weeks previously. This case also shows the importance of bacteriological examination before isolation is ended.

² In the United States a 20-volume solution of hydrogen peroxide has been and still is one which will yield 20 times its volume of oxygen, if decomposed by permanganate of potassium; but one-half of this oxygen is contributed by the permanganate, as it is likewise decomposed. The hydrogen peroxide (or dioxide) water, described in the United States Pharmacopœia for 1890, which will be official on January 1, 1894, is a 10-volume solution, and one in which the number of the volumes named denotes the amount of its own available oxygen. This 10-volume solution is therefore equivalent to the 20-volume solution described above. I have adopted in this article the Pharmacopœial manner of indicating the strength of the hydrogen peroxide solutions, and, therefore, the 50-volume solution of my paper of 1892 becomes here a 25-volume solution.

tion with a dilute solution of hydrogen peroxide, as illustrated by the last two cases.

It would take too long even to enumerate the various kinds of local treatment that have been used in diphtheria, but there are certain conditions to be fulfilled that will serve as a guide in our selection.

We need an agent that will kill the bacilli quickly, and will not injure the patient by its harmful or poisonous attributes. The first step in an investigation of this kind is to ascertain what will kill the organism in the laboratory, although it does not follow that the same result will be obtained in the throat. In the experiments made for me in the Biological Laboratory of the Massachusetts Institute of Technology with various germicides on the bacillus of diphtheria, I chose the short period of ten seconds for the limit of time during which they were allowed to exert their action, as the contact of the germicide with the membrane in the throat must necessarily be short.

The results of a few of the experiments were as follows: A saturated solution of carbolic acid did not kill the bacilli in ten seconds. A solution of hydrogen peroxide of between 12 and 25 volumes, containing $\frac{1}{4}$ to $\frac{1}{2}$ per cent. of acid respectively, killed the bacilli in ten seconds, but it took over a 50-volume nearly neutral solution of hydrogen peroxide to do the same work.

The ordinary hydrogen peroxide solutions offered for sale have a strength of 7.5 or 10 volumes or much less—some of these are neutral, others acid.¹ These weak solutions, whether neutral or acid, are not active germicides, judged by their effect upon the bacillus of diphtheria, an organism which is not so difficult to kill as the staphylococcus for instance, but the neutral solutions have far less germicidal power than the acid ones. I pointed out by some observations published last year,² the distinction that should be drawn between the nearly neutral and the acid solutions, but it is evident that this point needs further emphasis, particularly as the solutions of hydrogen peroxide are coming more into use, and neutral ones are made which are excellent for certain purposes, but which being nearly free from acids, have little germicidal value against the bacillus of diphtheria, *except in unusual strength*.

The strong hydrogen peroxide acid solutions, by which I mean strengths of 25 to 50 volumes or more, as already shown, are efficient germicides in the laboratory, and they have besides the special quality of breaking up and disintegrating certain portions of the diphtheritic membrane without injury to the healthy tissues, thus rendering the bacilli more accessible.

¹ It is interesting to note the importance of the mineral acids, especially hydrochloric acid; they are of value in the hydrogen peroxide solutions, and are good germicides when used alone; hydrochloric acid is, as we have seen, the active agent in the iron solutions, and is also a valuable germicide in the gastric juice.

² Boston Medical and Surgical Journal, September 29, 1892.

Having found a substance that has no poisonous properties, namely, a strong solution of hydrogen peroxide, that is shown to be an efficient germicide in the laboratory, let us see what it will do clinically. I was so situated that in most of the cases in which the diagnosis was carefully made by cultures, the strong hydrogen peroxide solutions were not used, and in most of the cases in which the peroxide treatment was used the cultures were not made. I have made some use, chiefly in 1892, of strong peroxide solutions, in seventy-four cases in all; sixteen of these died and fifty-eight recovered; but as, in most of these, the diagnosis was not based on cultures, it is impossible to state exactly how many were diphtheria and how many pseudo-diphtheria. In the sixteen cases that died the patients entered the hospital after they had been ill an average of five days, so far as I could learn. Eight of these died within one to three days after entrance. There was not much opportunity for treatment, and the hydrogen peroxide was omitted when the patients seemed too weak. Two entered the hospital on the last day of my service, and the strong solutions of hydrogen peroxide were employed on that day only. These patients died about two and four weeks later, respectively. In four cases the membrane was in or extended to inaccessible parts of the throat, and in but one of these was there temporary improvement. In the fifteenth case the patient had diphtheria (as shown by subsequent paralysis) and scarlet fever simultaneously. There was local improvement, but the child died about the fifteenth day of the disease. In the sixteenth case scarlet fever developed on the twelfth day of the disease, when the throat was nearly clear. The patient did well until the fifteenth day, then had suppurating glands and died on the nineteenth day of the disease.

In the four following cases, the diagnosis of which was based on cultures, the strong hydrogen peroxide acid solutions were used. The first two are cases of pseudo-diphtheria.

E. F., aged twenty years, entered the hospital on the second day of the disease. Thin, gray membrane on left tonsil and all along the arch of soft palate. Mr. Mathews found streptococci on cover-glass and in culture, but no bacilli. The membrane was cleared off completely with 50-volume solution of hydrogen peroxide applied with a swab, and this was followed by an application of chlorinated soda. Spray of 25-volume hydrogen peroxide solution every four hours. On the fifth day of the disease, but the third after treatment, the throat was clear. Recovery.

C. D., aged twenty-three years, consulted me on account of some slight difficulty, and, as a matter of routine, I looked in her throat, which was then clear. On the following day, I was much surprised to be sent for in some haste, and then found on both anterior pillars, tonsils and uvula, patches of membrane, which were one-sixteenth of an inch thick and could be removed with some difficulty with the edge of a teaspoon, but this caused bleeding. I removed most of the membrane with

a 25-volume hydrogen peroxide solution, but left the base of one patch on the soft palate, about one-fourth of an inch in diameter, fearing that further attempts to remove it might set up bleeding, as here the mucous membrane looked as if the surface had been etched off. As this patch was at a point readily accessible to a gargle, I left the patient at 1 P.M. with directions to use a dilute acid solution of hydrogen peroxide every half-hour and to follow this by a gargle of diluted solution of chlorinated soda. At my second visit, three and one-half hours later, I was much gratified to find the throat entirely clear of membrane. I saw the patient daily for some days, during which mild antiseptic sprays and gargles were used, but there was no return of the membrane. This was seen only at my first visit. No Klebs-Loeffler bacilli were found in cover-glass examination. Cultures showed streptococci and staphylococci.

We may look for better results in private practice than at the hospital, as in the former case patients are generally seen earlier.

In the two following cases of diphtheria, the diagnosis of which was based on cultures, there was partial use only of strong solutions of hydrogen peroxide, but even by this, good results were accomplished.

A. B., aged twenty-four years, entered the hospital on the second day of the disease. 4 P.M., membrane on right tonsil, thick in places, cartilaginous in character. Membrane also on left tonsil and left wall of pharynx. Klebs-Loeffler bacilli found on cover-glass and in culture. Strong hydrogen peroxide acid 25-volume solution was applied in spray, and 50-volume by syringe and swab, and the membrane removed except in points around anterior edge of left tonsil which were cartilaginous in character. The patient said there was less pain in swallowing a few minutes after the application of the peroxide than before, and after this application he ate his evening meal of eggs on toast, etc. At 9 P.M. the membrane had returned to some extent over its area of 4 P.M., but was not so thick and had not spread. Strong hydrogen peroxide was again applied. Spray of corrosive sublimate 1:10,000 given every two hours through the night. Large dose of bromide at night to prevent serious loss of sleep from frequent waking. The patient slept ten hours. No hydrogen peroxide solution was applied during the night, and the next morning the membrane was found to have spread rapidly over both sides and on to the back of pharynx in spite of the 1:10,000 corrosive sublimate that had been applied every two hours. There seemed to be some membrane in naso-pharynx. Strong hydrogen peroxide acid solution 25 and 50 volumes was then applied to the throat on swab. A solution of chlorinated soda, 1:6, was applied every two hours in spray. At 8 P.M., large dose of bromide. On fourth day of disease, membrane over same area as on the third day; 25- and 50-volume hydrogen peroxide applied morning and afternoon, followed by chlorinated soda. The membrane seemed to be kept from spreading or becoming thick if the applications of hydrogen peroxide were made every four hours, but otherwise it gained in thickness and somewhat in extent. Fifth day of the disease, general condition excellent. Membrane much less in extent and thinner. Hydrogen peroxide only twice during the day. Membrane seemed under control. Sixth day; the patient had eaten well before, but now had appetite. General condition excellent. Throat clearing. Two applications of hydrogen

peroxide, although this seemed hardly necessary, but it was done to prevent the possibility of relapse. Two per cent. spray of cocaine applied to throat prevented pain from the application of the peroxide. On the seventh day of the disease, and the fifth after entrance, a final application of peroxide was made. The patient left the contagious ward six days later. There was no cardiac weakness, no depression, and no paralysis.

M. L., aged eighteen years, entered the hospital February 25th, on the second day of the disease. His throat had the appearance of a follicular tonsillitis. On my first visit I found Klebs-Loeffler bacilli, micrococci and streptococci in a cover-glass examination. The next day Dr. Councilman obtained an almost pure culture of Klebs-Loeffler bacilli. At 1 P.M., there were two small patches of membrane on the right tonsil, the one an eighth by a quarter of an inch and the other an eighth of an inch in diameter. These were removed with six minims of a 25-volume hydrogen peroxide solution in syringe, and this was followed by an application of chlorinated soda. At 5 P.M., the throat was again cleared carefully with 25-volume hydrogen peroxide solution by swab and syringe, followed by an application of strong chlorinated soda on swab. At 9.30 P.M., the membrane was not visible except a thin, yellowish, translucent deposit over original area, namely, on right and left tonsil. This was cleared off with the hydrogen peroxide solution, and was followed by chlorinated soda solution. No hydrogen peroxide was used through the night, but a solution of chlorinated soda was applied every two hours. In spite of this, on the following morning the membrane had spread over the larger part of the right tonsil, and there was also a strip of membrane three-fourths by one-eighth of an inch on each side of the pharyngeal wall. This was cleared off again with 25-volume hydrogen peroxide solution on swab at 10.30 A.M. and again at 5.10 P.M. On the fourth day of the disease, only two applications of the peroxide were made, as the membrane was readily controlled, and on the fifth day one final application of the peroxide was made. On the sixth day of the disease, and fourth after entrance, the throat was clear. Patient felt well and asked if he might get up. Discharged after being kept under observation ten days longer. There was no cardiac weakness, no depression, and no paralysis.

In these two cases the strong solution of hydrogen peroxide was used only two or three times in the twenty-four hours, and the membrane returned during the long intervals of several hours when it was not applied, in spite of the use of corrosive sublimate or chlorinated soda every two hours. These cases had only a partial peroxide treatment. In both instances, the condition of the patient was excellent throughout the illness. These two cases suggest that by early local treatment with peroxide we may diminish the generation and absorption of poison from the bacilli.

I have found nothing that will remove the membrane so well as the strong solutions of hydrogen peroxide.

The *drawbacks* of the strong solutions of hydrogen peroxide¹ consist,

¹ I give some details concerning the strong hydrogen peroxide solutions, as they are a novelty. Physicians and chemists told me that even 25-volume solutions were impracticable

first, in the fact that the acid solutions, which are stronger germicides, cause pain, due to the acid, which lasts about one minute. Some patients object to this very much; others, including children, will permit the use of a 50-volume solution with little fuss. In private practice, I recall a young lady who applied the 50-volume solution to her own throat on a swab and used it more frequently than I had directed. On another occasion I suggested in consultation that cocaine be first applied to the throat, but the physician in attendance said it was unnecessary, as the patient, a child three and one-half years old, did not mind the 50-volume solution, which he had been using in spray. The discomfort is due to the acids rather than the hydrogen peroxide; if the solutions are neutralized the discomfort is largely obviated. We may disguise the acid by adding sugar, as in lemonade, showing that it is the acid taste that is disagreeable rather more than the so-called irritation. Instead of adding sugar we may apply cocaine to the throat before we use the hydrogen peroxide solution. The amount of acid in the 25-volume solution which I used was $\frac{1}{2}$ per cent., in the 50-volume 1 per cent. This is far less than the amount of acid in the chloride of iron solutions, for, as already stated, the tincture contains from 2.5 per cent. to 3.4 per cent. of hydrochloric acid, and the solution of the chloride of iron from 5.4 per cent to 7.4 per cent. of hydrochloric acid.

Second. Strong solutions of hydrogen peroxide¹ have not been easily procured, nor do they bear transportation well, but these inconveniences may be readily surmounted. The apothecary or physician has merely to evaporate a 10-volume solution in a shallow, open dish, over a water-bath, or on a range or stove, to obtain a solution of either about 25 or 50 volumes.² The initial solution should not be too acid, the dish should not be of metal and should be free from organic matter.

or impossible, but as the caution came after I had had a 100-volume solution I was not dismayed.

Unlike chlorine and chlorinated soda, corrosive sublimate, if desired, may be mixed with hydrogen peroxide; citric or tartaric acid should be added to prevent the precipitation of albuminate of mercury in the throat.

It gives me pleasure to again express my indebtedness to Professor H. P. Talbot, of the Massachusetts Institute of Technology, for his assistance in the study of hydrogen peroxide.

¹ The stability of the strong solutions and the precautions to be used for keeping them I have already described in a former article. As soon as the properties of strong solutions are more widely known and it is appreciated that they may be obtained without much difficulty, they will, I believe, find other uses than that of a local application in diphtheria. They should not, of course, be employed in closed cavities, as the oxygen liberated might cause pressure.

² To be more precise, a 25 or 50-volume solution may be obtained by evaporating a 10-volume solution to $\frac{1}{5}$ or $\frac{1}{6}$ of its bulk respectively. The loss of the hydrogen peroxide is usually less than 10 per cent. in the former case, and about 20 per cent. in the latter. The temperature being the same, the loss seems to be less when the hydrogen peroxide is evaporated quickly than when the process is carried out more slowly. One teaspoonful of a 50-volume solution is ample with which to begin the treatment. The strong solutions should be kept in a cool place.

By evaporating 200 c.c. of a 11.5-volume solution I have obtained a 275-volume solution. A drop of this applied to my tongue caused momentary smarting.

A 10-volume solution of hydrogen peroxide may be tested in the following way: One drachm

Third. Hydrogen peroxide is a bleaching agent and should not be brought into contact with the hair or with colored fabrics, but it does not injure white cotton or linen. One should avoid getting it on the fingers, as it may, after a few minutes, whiten a thickened epidermis and cause a sensation of pricking.

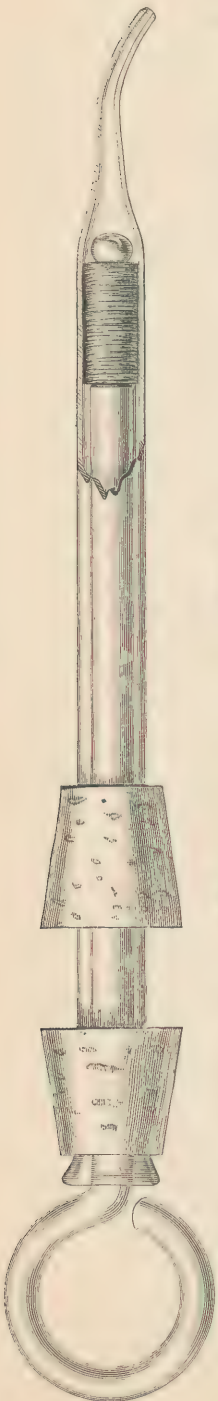
The *advantages* of the strong hydrogen peroxide solutions are that they are good germicides and are not poisonous nor harmful to the mucous membrane; they cleanse a foul throat and break up and disintegrate certain portions of the diphtheritic membrane, thus rendering the bacilli more accessible. They likewise assist in diagnosis, for when the hydrogen peroxide, even in weak solution, is applied to the throat where there is any trace of membrane, it causes it to assume a white color from the presence of fine foam which is made by the liberation of the oxygen gas. It thus becomes a useful agent in detecting spots of membrane earlier than they would be apparent in any other way, and thus indicates the areas to which the treatment should be directed. With this end in view, the throat may be sprayed or the mucous membrane may be swabbed with dilute hydrogen peroxide. It is known that corrosive sublimate to a considerable extent is inhibitory rather than germicidal in its action, but it would be difficult to conceive of a merely inhibitory action on the part of hydrogen peroxide, as this substance is so readily decomposed.

No rule can be given for applying these solutions that will cover all cases. In a general way it may be said that the strong solutions of hydrogen peroxide containing about $\frac{1}{2}$ per cent. of acid, made up chiefly of hydrochloric or sulphuric acid, should be gently but thoroughly applied every four hours during the night and more frequently during the day for the first few days. The 25-volume solution may be used in spray; the 50-volume may be applied, a drop or two at a time, on a swab until the membrane is removed or much diminished, or in certain cases the 50-volume solution may be applied with the syringe. Even a stronger solution than 50 volumes may be used for resistant membranes. It is well to use cocaine before applying the peroxide. By the help of bromide at night, the patient loses very little sleep in being aroused for the local treatment. Every precaution should be taken to spare the patient's strength, and it is not necessary that the head should be raised from the pillow while the applications are being made.

As the bacilli are not limited to the diphtheritic membrane, antiseptics should be brought into contact with other portions of the throat

of it diluted with about an ounce of water and acidified with about three drachms of dilute sulphuric acid will dissolve and decompose three grains of permanganate or potassium (in crystals) and leave a colorless solution. If the strength is less than 10 volumes the solution will finally be of a bright-red color.

FIG. 2.



and nose than those covered with membrane, by such means as sprays and gargles, as a prophylactic measure.

The accompanying cuts show the instruments which I have designed for making applications to the throat; but any good atomizer, not of metal, that will reach the desired spot conveniently, or a swab made by twisting a small piece of absorbent cotton about the end of a small stick, may be used.

FIG. 1.

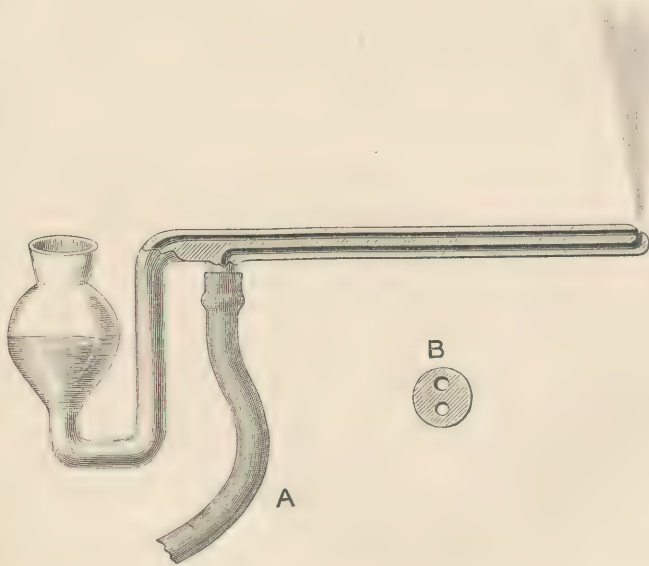


FIG. 3.

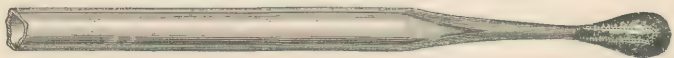


FIG. 1.—A, rubber tubing to hand-bulb. The cut is one-half size except the section of the tube at B, which is full size. The bulb in the drawing should have more the shape of a top, and when of such shape it can be placed on its side without losing any of its contents if it is not more than half full. If the tubing, A, which joins the rubber hand-bulb to the atomizer is only about one inch long, the atomizer can be worked with one hand. It will be noticed that the straight tube of the atomizer is unusually long—more than four inches from the rubber tubing to the tip.

FIG. 2.—The *syringe* is of glass one inch longer than the drawing, otherwise this is the full size. The walls of the syringe beyond the piston are thick, and the tip is smooth, having been rounded in a flame. The form is such that it can reach any part of the throat within sight. The corks are now replaced by glass projections. The packing may be of cotton or asbestos. The cost of the syringe is trifling.

FIG. 3.—The *swab* is eight inches long, but otherwise the drawing is full size.¹

¹ These are made by P. J. McElroy, East Cambridge, Mass., U. S. A.

By means of this atomizer (Fig. 1) the spray may be sent in three directions, up and right and left, in the throat without taking it out of the mouth, but merely turning it in the hand.

The syringe (Fig. 2) may be pushed through the false membrane and a drop or two of solution pressed out, the oxygen then generated underneath a *thick* membrane will lift off large pieces of it. In this way large numbers of bacilli are removed, the poison from which might otherwise be swallowed and absorbed.

The swab (Fig. 3) used to apply the solution consists of a small glass tube drawn out at one end into a smaller rod, about which sufficient absorbent cotton has been twisted to hold two or three drops of liquid. The end of the rod has been rounded in a flame and made slightly bulbous, as shown by the dotted line; by this device the cotton is held firmly.

The sterilized swab and its holder, seven inches long, which I used for taking specimens from the throat are shown in the woodcut (Fig. 4), which is about one-half size. After the swab has been rubbed over the throat it is replaced in the tube of thick glass, which is stopped with sterilized cotton. A small piece of this having been previously torn off is moistened with a few drops of water and placed above the stopper to prevent the specimen from drying. The tube is then closed with a cork to prevent evaporation. There should be no delay in taking a swab from the throat, and the treatment should then be applied without waiting for the result of the cultures.

I have found it difficult to obtain some common germicides—not only hydrogen peroxide—of the strength which they purport to be. This leads me to emphasize the need of caution concerning the quality of the remedies we employ. Physicians may well take a lesson in therapeutics from the surgeons, for in antiseptic surgery, which is largely therapeutics, they set us an example of painstaking care in the use of remedies that we should do well to follow. If in surgery, where the conditions are comparatively simple, so much pains must be taken, how much more careful should we be when the problem is more complex. When in the selection and application of our remedies we approach the standard antiseptic surgery has set for us, we shall hear less about the inefficacy of drugs.

Diphtheria usually begins on the tonsils, and, to avoid serious consequences—for instance, those resulting from the spread of the membrane to the neighboring air-passages—no moments should be lost before beginning treatment. Until we have found something that will find

FIG. 4.



and kill all the bacilli at a single blow, any local treatment must be frequently applied to be efficient, as the bacilli reproduce themselves in a very short period. From these frequent applications during the early days of the disease I see, at present, no appeal. The use of the strong hydrogen peroxide solutions reduces the number of applications to a minimum, as the more thoroughly the membrane is disintegrated and removed the less frequent is the necessity for treatment and the shorter its duration.

In those cases that are first seen several days after the onset of the disease, and when the patient has become weakened by the poison generated by the bacilli, we must weigh carefully the loss of strength resulting from frequent applications, especially in very young children, against the gain to be derived from the removal or destruction of the bacilli. Further, if the patients have been ill some days when first seen, the chances of recovery are much diminished, and in some cases no treatment as yet at our command is of avail; just when the physician shall renounce all hope of aid from local treatment each one must, of course, decide for himself in the individual case. The usefulness of good local treatment is in direct ratio to the stage of the disease, the accessibility of the membrane, the age and strength of the patient, and the ability of the practitioner to apply it with the least tax on the patient's strength combined with the greatest destruction of the bacilli.

I beg you not to go away from here with the impression that diphtheria can always be cured by strong hydrogen peroxide solutions. I maintain only that when properly used they are more efficient and less harmful than any other treatment I know of. Under their use all of the few cases that I have thus far seen early in the disease, recovered.

As already stated in the opening of this paper, there were 36,553 deaths from diphtheria and croup in Massachusetts from 1871 to 1890, inclusive. Rather more than one-half of these, 19,310, occurred within a very limited area, that is, within the area of the twelve cities, or those fractions of them represented by the nine¹ black spots on the accompanying map. During these twenty years about 43 per cent. of the population was to be found in these cities, and 53 per cent. of the deaths from diphtheria and croup during this time occurred in them. Further, it is of interest to note that the greater part of these deaths occurred during four months of the year, namely, from October to January, inclusive. These are suggestive facts when considered from the standpoint of prevention. It is highly important for each city and large town to have a suitable hospital for contagious diseases, and also to offer facilities for bacteriological examinations in those diseases in which false membranes develop. In smaller communities it would seem desirable to extemporize a hospital during an epidemic.

¹ Four cities—Boston, Cambridge, Chelsea, and Somerville—are contiguous.

Diphtheria seems to me to be chiefly a hand-to-mouth or mouth-to-mouth disease; its cause is tenacious of life, especially in damp places, and is not killed by cold, but is killed by sunlight. The



period of incubation after the bacilli have reached the mucous membrane is probably in some cases not days but hours only. With the improved means of diagnosis at our command, by early isolation, and the co-operation of intelligent citizens with the Boards of Health, it may become one of the most preventable of diseases, and I hope that before many years have elapsed we shall see diphtheria considerably diminished in our State as well as elsewhere. The members of this Society can do much to further this end. The best defence against this disease is educated public opinion.

SUMMARY.

1. The necessity of cultures as a means of early diagnosis.
2. The coincidence of diphtheria and other diseases.
3. The bacteriological examination of all patients ill with scarlet fever, typhoid fever, measles, or other disease, who have membranous throats.
4. The bacteriological examination of specimens from the throats of all diphtheria patients before isolation is ended.
5. Seven and one-half- [known at present in the United States as fifteen-] volume solutions of hydrogen peroxide are weak germicides.
6. The advantages of strong hydrogen peroxide solutions, locally, in diphtheria. The substitution of harmless and more efficient for harmful or inefficient local treatment.
7. The importance of frequent, early local applications.

NOTE.—Dr. John F. Young, of Newburyport, Mass., was present when this paper was read, and ten days later had a case of diphtheria, in which he used the strong hydrogen peroxide solutions. I heard of it by chance some weeks afterwards, as the patient was the child of an acquaintance. In reply to my inquiries, Dr. Young kindly wrote me about the case. With his permission I quote his letter almost in full:

“My patient was a bright and sensible girl aged ten years. On the morning of the 24th of June she complained of headache and sore-throat; I saw her for the first time about four o'clock that afternoon. There was some stiffness of the neck and some swelling on each side at the angle of the jaw. The tonsils and arches of the palate were red and swollen. There was considerable fever and also a good deal of dizziness when the patient sat up in bed. Small dose of calomel, as bowels were somewhat confined, and boric acid gargle.

“Saw her next morning, 25th, about ten o'clock, when tonsils and arches of palate nearly up to uvula were covered with a thick, grayish exudation, the cervical glands were more swollen, and more constitutional disturbance was present than on first visit. Treatment with peroxide of hydrogen was now begun after evaporating the solution to one-quarter its original bulk; and, as the patient complained of no very

disagreeable sensation from its use, it was ordered to be applied in the form of a spray every hour. Saw the patient again about 7 P.M. There had been no extension of exudation, no other change noticed, except that the exudation looked thicker and more swollen. Directed that spray be used every two to three hours through the night.

"On the morning of the 26th, no considerable change in appearance of throat, no extension, but patient had decidedly less trouble (dizziness) on sitting up, and expressed herself as feeling better. Evening about the same.

"27th, A. M. Patches on tonsils and palatine arches appeared to be more loosely attached and also thicker than before. A patch of exudation (rather thin) about the size of a finger-nail, was seen opposite the last inferior molar on right side, and another on the front of soft palate near roof of mouth on left side. The peroxide was now applied by means of a swab and repeated again toward evening by myself, the spray being used as before by the nurse. During the evening on swabbing the exudation in the mouth it seemed to melt away, leaving raw and bleeding surfaces, and the original patches to diminish in size considerably, and on the morning of the 28th it came off almost at the first touch of the swab. The surfaces left bare were raw and bleeding, and a spray of carbolic acid and lime-water was now substituted for the peroxide and used every hour. No reappearance of patches at the evening visit.

"29th, A. M. White patches again covered tonsils and arches of palate, not so thick, however, as before, and were removed entirely by two swabbings with peroxide on same day, and did not again return. Spray of carbolic acid and lime-water was continued for the next two days, when one of boric acid was substituted for it.

"By the 4th of July the throat was looking almost well. At this time a slight nasal intonation was noticed, and after this there was some tendency to regurgitation of liquids through the nose. (This became more marked later.)

"It seemed to me that the peroxide had a decidedly beneficial effect, the constitutional symptoms growing less and less every hour from the very start. The general treatment of the patient consisted in the administration of iron, brandy and milk every three hours, and meat juice midway between feedings of milk and brandy."

The noteworthy points in this case are, first, the effect of the local treatment by strong hydrogen peroxide solutions on the patient's general condition; second, the disappearance of the membrane under the use of this application; its reappearance when carbolic acid and lime-water were substituted, and its final disappearance when the strong hydrogen peroxide was resumed.

I wish to express my appreciation of the courtesy and kindness that have been extended to me in the chemical and biological laboratories of the Massachusetts Institute of Technology, by Professor T. M. Drown and Professor William T. Sedgwick, while I was carrying on some of the investigations connected with this paper.

The American Journal OF THE MEDICAL SCIENCES.

MONTHLY, \$4.00 PER ANNUM.

WITH 1893 THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES enters upon its seventy-fourth year, still the leader of American medical magazines. In its long career it has developed to perfection the features of usefulness in its department of literature, and presents them in unrivalled attractiveness. It is the medium chosen by the leading minds of the profession on both sides of the Atlantic for the presentation of elaborate Original Articles; its Reviews are noted for discernment and absolute candor, and its Classified Summaries of Progress each month present an epitome of medical advances gleaned by specialists in the various departments. According to unquestionable authority, "It contains many original papers of the highest value; nearly all the real criticisms and reviews which we possess, and such carefully prepared summaries of the progress of medical science and notices of foreign works that from this file alone, were all other publications of the press for the last fifty years destroyed, it would be possible to reproduce the great majority of the real contributions of the world to medical science during that period."

The Medical News.

WEEKLY, \$4.00 PER ANNUM.

BY KEEPING closely in touch with the needs of the active practitioner, THE NEWS has achieved a reputation for utility so extensive as to render practicable its reduction in price from five to **Four Dollars** per annum. It is now by far the cheapest as well as the best large weekly medical journal published in America. Employing all the recognized resources of modern journalism, such as the cable, telegraph, resident correspondents, special reporters, etc., THE NEWS furnishes in the 28 quarto pages of each issue the latest and best information on subjects of importance and value to practitioners in all branches of medicine. Its numerous departments are designed to subdivide and present its material in the most attractive and convenient manner.

In a word THE MEDICAL NEWS is a crisp, fresh, weekly newspaper, and as such occupies a well-marked sphere of usefulness, distinct and complementary to the ideal monthly magazine, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

The Year-Book of Treatment for 1893

Gives a classified summary and review of the real advances in treatment made during 1892 in all departments of the science of medicine. Price, \$1.50; or in combination with either or both the above journals, 75 cents.

The Medical News Visiting List for 1893

Published in four styles: Weekly, dated, for 30 patients; Monthly, undated, for 120 patients per month; Perpetual, undated, for 30 patients weekly per year; Perpetual, for 60 patients weekly per year. The first three styles contain 32 pages of important data and 176 pages of assorted blanks; the 60-patient perpetual consists of 256 pages of blanks. Price, each, \$1.25. In combination with either or both above periodicals, 75 cents. Or, JOURNAL, NEWS, VISITING LIST and YEAR-BOOK, \$8.50. Thumb-letter index for VISITING LIST, 25 cents extra.

LEA BROTHERS & CO., PUBLISHERS, PHILADELPHIA, 706 & 708 Sansom Street.